

REMARKS

Claims 1-44 are pending. Claims 1-34 and 40-44 are withdrawn from consideration. Claims 35-39 currently stand rejected. Claims 46 and 47 are added by this Amendment.

Rejections under 35 USC § 112, second paragraph

The Office has rejected claims 35, 37 and 38 under 35 USC § 112, second paragraph as allegedly being indefinite. The Office alleges that claim 35 is unclear in the use of the phrase "a first composition" in referring to component (a) of the immunogenic composition. Claim 35 is currently amended to delete the phrase "a first composition comprising". In view of the amendment, Applicants believe that the claim is definite and request that the Office withdraw its rejection of the claim under 35 USC § 112, second paragraph.

The Office alleges that claim 37 is indefinite in the use of the phrase "VSV is non-replicating". Claim 37 is currently amended to replace the phrase "VSV is non-replicating" with "VSV is not replication competent". Support for this amendment can be found at paragraph [0050] of the published application. In view of the amendment, Applicants believe that the claim is definite and request that the Office withdraw its rejection of the claim under 35 USC § 112, second paragraph.

The Office alleges that claim 38 is indefinite for similar reasons as claim 35. In view of the amendment to claim 35, Applicants believe that claim 38 is definite and request that the Office withdraw its rejection of the claim under 35 USC § 112, second paragraph.

Rejections under 35 USC § 112, enablement

The Office has rejected claims 38 and 39 under 35 USC § 112, first paragraph as allegedly lacking enablement. Specifically, the Office alleges that the claims, "while being enabling for a cytokine that can induce an antigen specific immune response to antigen is not enabled for any cytokine", (Office action, p. 3, paragraph 4, lines 2-3). Claim 38 is amended to include the phrase "wherein the cytokine enhances the immune response when administered together with the antigen". Support for this amendment can be found at paragraph [0079] of the published specification, which further lists representative cytokines that can be used to enhance the immune response. No new matter is introduced in this amendment. Claim 39 is dependent of claim 38.

To practice the claimed invention, one skilled in the art need not conduct experimentation which requires "ingenuity beyond that to be expected of one of ordinary skill in the art", since the

specification provides a list of pro-immune response cytokines as well as references that teach the respective activities of cytokines at paragraphs [0079] – [0083] of the published specification, thus providing guidance to the artisan in the practice of the claimed invention.

The Office acknowledges in the Office action (p. 3, paragraph 4, lines 2-3) that the specification is “enabling for a cytokine that can induce an antigen specific immune response”. In view of the amendment to claim 38, Applicants submit that claims 38 and 39 are enabled and request that the Office withdraw its rejection of those claims under 35 USC § 112, first paragraph, enablement.

Applicants are currently introducing new claims, numbered 46 and 47, which are dependent of claims 38 and 39 respectively. These new claims specify that the cytokine is interleukin-12 (IL-12). Support for these new claims can be found at paragraph [0083] of the published specification. No new matter is introduced in this amendment.

Rejection under 35 USC § 102(b)

The Office has rejected claims 35-37 under 35 USC § 102(b) as allegedly being anticipated by Rose et al (WO96/34625) (“Rose”). Rose is cited for allegedly teaching “an immunogenic composition comprising a plasmid DNA expression vector with foreign DNA encoding antigens and NPL proteins and foreign antigen are introduced into same cells to result in assembly of recombinant immunogenic VSV”, (Office action, p. 4, last 5 lines).

Applicants traverse. The claimed invention requires an immunogenic composition comprising: (i) a plasmid containing DNA encoding an antigen, (ii) a recombinant vesicular stomatitis virus (VSV) containing a nucleic acid sequence encoding the antigen, and (iii) the composition induces an antigen-specific immune response to the antigen in a mammalian subject. The Office, in its citation of Rose, has failed to establish a *prima facie* case of anticipation since it failed to show that each and every element of the claimed invention is disclosed in Rose. Rose fails to teach the combination of a plasmid containing the antigen sequence and the VSV containing the antigen sequence.

It appears the Examiner has misinterpreted the teachings of Rose with respect to the disclosure of plasmids. In the portions of Rose cited by the Examiner, Rose uses plasmids as DNA vectors for the expression of VSV N, P and L proteins, which are used in the recovery of recombinant replicable VSV. Rose does not disclose the use of plasmids to express antigens as a component of an immunogenic composition.

Specifically, Rose makes a clear distinction between the VSV N, P and L proteins and the foreign antigen DNA (see Rose, p. 38, lines 17-20). Rose teaches “expression vectors containing DNA encoding the N, P, and L, proteins, and the vesiculovirus (-) DNA containing the foreign DNA”, (Rose, p. 38, lines 30-32). Rose fails to teach an immunogenic composition comprising both an expression plasmid containing antigen DNA and a VSV vector containing antigen coding sequence. Instead, Rose teaches expression plasmids encoding VSV N, P, and L proteins and the use of the resulting recovered VSV as a vector encoding the foreign DNA (see for example Rose at p. 40, lines 4-37 bridging p. 41; p. 42, lines 30-37 bridging p. 43; p. 38; p. 123-132, as cited by the Office in the Office action, p. 4, last line – p. 5, first line).

Since Rose fails to teach each and every element of the claimed invention, Rose fails to anticipate claims 35-37. Applicants therefore request that the Office withdraw its rejection of the claims under 35 USC § 102(b) over Rose.

Rejections under 35 USC § 103(a)

Claims 35-37

The Office has rejected claims 35-37 under 35 USC § 103(a) as allegedly being unpatentable over Haglund et al (2002, J. Virol. 76:7507-7517) in view of Ramshaw et al (2000, Immunology Today 21:163-165) (“Ramshaw”).

The Office cites Haglund for allegedly teaching a “prime-boost regimen using DNA vaccine vectors (plasmid expression vectors as vaccine) and viral vaccine vectors[,] in particular [a] VSV vector along with a heterologous vector (eg. Vaccinia virus vector) coding the same antigen”. The Office acknowledges that Haglund fails to teach “a plasmid vector in his prime boost composition comprising VSV”, (Office action, p. 5, paragraph 5). Ramshaw is cited for allegedly teaching a “prime-boost vaccine compris[ing] DNA vaccines and attenuated poxvirus vectors encoding similar antigens”, (Office action, p. 5, para. 6, lines 2-4).

Applicants traverse. Applicants respectfully submit that the Office’s characterization of Ramshaw is inaccurate. Ramshaw emphasized “two important principles of effective prime-boost immunization: (1) the importance of DNA vaccines as priming vehicles and attenuated viruses as boosters and (2) the nature of the boosting virus”, (Ramshaw, p. 164, col. 3, lines 8-12). Regarding the nature of the boosting virus, Ramshaw states that the “viral vectors, particularly those that are, in some way, unable to replicate in mammalian hosts [e.g. fowlpoxvirus and modified vaccinia virus Ankara strain] have *significant advantages* over

alternative immunization strategies", (Ramshaw, p. 163 col. 1, para. 2, lines 6-11; *emphasis added*).

The claimed invention requires as one of its elements a vesicular stomatitis virus as a viral vector containing a nucleic acid encoding an antigen. In contrast, Ramshaw teaches only two viral vectors, FPV and MVA – both of which are poxviruses (DNA viruses) -- neither of which is VSV, which is not a poxvirus (rather a negative stranded RNA virus).

Furthermore, Ramshaw teaches away from the claimed immunogenic composition combination. Ramshaw states that “[e]ither reversing the order of immunization or changing the strain of [vaccinia virus] from MVA or the closely related NYVAC strain to the WR strain (which replicates extensively in mice), resulted in a failure of protection”, (Ramshaw, p. 164, column 3, lines 13-17) and that other alternative protocols “largely produced disappointing results”, (*ibid* at lines 18-27). The claimed invention does not follow the prescribed order of Ramshaw and it uses a different viral vector (non-vaccinia), which, according to Ramshaw, would result in a failure of protection or disappointing results. Thus, Ramshaw teaches away from the claimed invention.

Regarding Haglund, Haglund describes the use of a VSV-env (and also VSV-gag in separate experiments) as a priming vaccine, boosted with vaccinia virus (VV)-env (or VV-gag, in the respective separate experiments) (see Haglund at Discussion, p. 7513, first paragraph). Haglund then compares the reverse scenario, in which the VV-antigen construct is used as the priming vaccine and the VSV-antigen construct is used as the boost, and observed that the immune “responses are reduced about 25 to 30% compared to the response obtained when mice are vaccinated with VSV-env and boosted with vPE16”, which is the VV-env construct, (Haglund, p. 7509, column 2, paragraph 3, last line). Haglund does not teach, motivate or suggest the use of a DNA plasmid construct bearing the antigen-encoding sequence.

Looking at Haglund in view of Ramshaw, these references fail to teach, motivate or suggest to one of ordinary skill in the art, an immunogenic composition comprising the combination of a VSV vector and DNA plasmid vector, each encoding the same antigen. Haglund and Ramshaw each describe the inclusion of a poxvirus vector in an immunogenic composition. Thus, the combination of Haglund and Ramshaw actually teaches away from the claimed invention, which does not require the use of a poxvirus vector. As a result, one of ordinary skill in the art could not predict the claimed invention by reading Haglund in view of Ramshaw.

Claims 38-39

Claims 38 and 39 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over Haglund in view of Ramshaw as applied to claims 35-37, in further view of Gerhardi et al (2001, *Histol. Histopathol.* 16: 655-667) ("Gerhardi").

The Office cites Gerhardi as allegedly teaching "vaccines with cytokines as an adjuvant enhance cellular immune responses to pathogens during prime-boost vaccination regimens", (Office action, p. 6, paragraph 5).

Applicants traverse. Gerhardi fails to cure the deficiencies of Haglund and Ramshaw. Since claims 38 and 39 are dependent on claims 35 and 38 respectively, Applicants submit that claims 38 and 39 are not obvious over Haglund in view of Ramshaw in further view of Gerhardi.

In consideration of the arguments presented above, Applicants believe that the claims are patentable under 35 USC § 103(a) and therefore request that the Office withdraw its rejection of the claims under 35 USC § 103(a).

CONCLUSION

In view of the foregoing, Applicants believe that all rejections have been overcome and claims 35-39, 46 and 47 are in a condition for allowance. The Examiner is invited to call the undersigned Agent to discuss any remaining issues.

Respectfully submitted,



Joseph E. Zahner
Agent for Applicants
Reg. No. 48,224

Wyeth
Patent Law Department
Five Giralda Farms
Madison, NJ 07940
Tel. No. (973) 660-6613